

Claims

1. Microcapsules suitable for administration to a human or animal which microcapsules harbour cells containing a polynucleotide construct, said construct comprising:
- 5 (a) a promoter which is responsive to ecdysone or an analog thereof and which is operably linked to a coding sequence for a nitric oxide synthase (NOS) or a functional variant thereof; or
- 10 (b) a promoter operably linked to one or more tetracycline operator site sequences and a coding sequence in that order, wherein the coding sequence encodes a nitric oxide synthase (NOS) or a functional variant thereof.
2. Microcapsules according to claim 1, wherein the construct is
- 15 incorporated into a vector.
3. Microcapsules according to any one of the preceding claims, wherein the microcapsules comprise at least one of alginate, acrylic, hydroxyethyl-methacrylate-methyl-methacrylate, polyphosphazene or agarose.
- 20 4. Microcapsules according to any one of the preceding claims, wherein the microcapsules contain an average of from 1 to  $1 \times 10^7$  cells.
5. Microcapsules according to any one of the preceding claims, which
- 25 are the microcapsules are substantially spherical microcapsules or substantially cylindrical microcapsules.
6. Microcapsules according to claim 5 which are substantially spherical microcapsules having an average diameter of from 0.01 to 4.0 mm.
- 30 7. Microcapsules according to claim 5 which are cylindrical

microcapsules having an average length of from 0.1 to 20 mm and an average outer diameter of from 0.1 to 4.0 mm.

5           8.       Microcapsules according to any one of the preceding claims for use in a method or treatment of the human or animal body by therapy.

          9.       Microcapsules according to claim 8 for use in the treatment of a condition associated with deficient NO production.

10          10.       Use of microcapsules according to any one of claims 1 to 7 in the manufacture of a medicament for use in the treatment of a condition associated with deficient NO production.

15          11.       A pharmaceutical composition comprising microcapsules according to any one of claims 1 to 7 and a pharmaceutically acceptable carrier or diluent.

          12.       A method of delivering microcapsules to a host comprising administering microcapsules according to any one of claims 1 to 7.

20          13.       A method of treating a host suffering from a condition associated with deficient NO production, which method comprises administering ecdysone or an analog thereof to a host which harbours microcapsules as defined in any one of claims 1 to 7.

25          14.       A product containing microcapsules according to any one of claims 1 to 7 and ecdysone or an analog thereof as a combined preparation for simultaneous, separate or sequential use in the treatment of a condition associated with deficient NO production.

30          15.       A polynucleotide construct comprising:  
          (a)       a promoter operably linked to a coding sequence, wherein the

promoter is responsive to ecdysone or an analog thereof and the coding sequence encodes a nitric oxide synthase (NOS) or a functional variant thereof; or

- 5 (b) a promoter operably linked to one or more tetracycline operator site sequences and a coding sequence in that order, wherein the coding sequence encodes a nitric oxide synthase (NOS) or a functional variant thereof.

10 16. A polynucleotide construct according to claim 15, wherein the NOS is human inducible NOS.

17. A polynucleotide construct according to claim 15, wherein the NOS is human neuronal NOS.

15 18. A polynucleotide construct according to claim 15, wherein the NOS is human endothelial NOS.

20 19. A polynucleotide construct according to any one of claims 15 to 18, wherein the promoter in part (a) comprises a minimal promoter and an element or elements which is/are responsive to ecdysone or an analog thereof.

20. A polynucleotide construct according to any one of claims 15 to 18, wherein two operator site sequences are present in part (b).

25 21. A vector which incorporates a polynucleotide construct as defined in any one of claims 15 to 20.

22. A cell which harbours a polynucleotide construct according to any one of claims 15 to 20 or a vector according to claim 21.

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23. A cell according to claim 22 which harbours a construct as defined in

part (a) of claim 15 and which is capable of expressing a functional ecdysone receptor.

5           24.     A cell according to claim 23, wherein the functional ecdysone receptor comprises a heterodimer of the ecdysone receptor (EcR) or functional variant thereof and the human retinoid X receptor (RXR) or functional variant thereof.

10           25.     A cell according to claim 22 which harbours a construct as defined in part (b) of claim 15 and which is capable of expressing the tetracycline repressor protein or a functional variant thereof.

          26.     A process for preparing microcapsules comprising encapsulating cells according to any one of claims 22 to 25.